DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Minneapolis District
240 Hennepin Avenue
Minneapolis MN 55401-1999
Telephone: 612-334-4100

T2088 M

September 21, 1998

cc: HFI-35/FOI Staff
DWA

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Refer to MIN 98 - 52

Gary L. Swanson
President
Geneva Laboratories, Incorporated
1001 Proctor Drive
Elkhorn, Wisconsin 53121

Dear Mr. Swanson:

During our inspection of your contract testing laboratory in Elkhorn, WI, our investigators documented deviations from Good Manufacturing Procedures for Finished Pharmaceuticals (Title 21, Code of Federal Regulations, Parts 210 and 211). These deviations cause products tested and released by your laboratory to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food Drug and Cosmetic Act (the Act).

Deviations from the GMP observed during our inspection include, but are not limited to, the following:

1. Failure to properly validate the sterility testing of products in that

   A. Validations of the [redacted] system were not performed in conformance with the manufacturer's direction;
   B. Microorganisms used to challenge the system did not include non-ATCC microorganisms such as would be expected to be found in

products being tested, for instance, environmental monitoring isolates or microbial contaminants recovered from test products;

C. The number of validation runs was not adequate to demonstrate the reliability of the system.

2. There is no backup system for identification of microorganisms.

3. Despite a significant level of out-of-specification results for product sterility tests, you failed to conduct failure investigations in conformance with Geneva Laboratories Standard Operating Procedures and investigations did not study many potential causes for the failures, including:

   A. No sterility testing was performed on the water used to hydrate test articles;
   B. Non-viable particulate measurements were not taken in the sterility testing rooms to assure the rooms were maintained to the Class 100 specification;
   C. No monitoring of clean room personnel for environmental contamination was performed;
   D. There was no monitoring of the differential air pressure between gowning and media prep rooms;
   E. Large holes and cracks in the wall of the sterility test area were left unrepaired;
   F. There was no record of silicon repairs to the [redacted] air filters to assure the limit for silicon had not been exceeded;
   G. [redacted] air flow filters were not replaced as scheduled in Geneva Laboratories Standard Operating Procedures.

4. Storage temperatures of media and Biological Indicators were not monitored.

These and other items were listed on the form FDA-483 issued to and discussed with you at the conclusion of our inspection on June 9, 1998.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence with

each requirement of the Good Manufacturing Practices regulations. Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts. Additonally, pending Antibiotic Form 6, NDA, ANDA, or export approval requests may not be approved until the above violations are corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Possible action includes injunction.

You should notify this office in writing within 15 working days of receipt of this letter of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be accomplished within 15 working days, state the reason for the delay and the time within which corrections will be completed.

Your reply should be directed to Compliance Officer Lawrence R. Murphy at the address indicated on the letterhead.

I acknowledge receipt of your written response to the items cited on the FDA form-483 which was sent to Mr. Steven Masiello, Center of Biologics Evaluation and Research, by [redacted] on July 31, 1998.

Please include any additional responses to these items with your response to this letter. Also include additional information such as:

* A description of the back-up system you are using for the [redacted] system;
* A summary of the study you conducted on the microbial contaminant analysis of DI water;
* Specify the time frame for periodic re-certification of the clean room by an outside consultant;
* Report the status of the repairs to the clean room;
* Update the status of personnel environmental testing (i.e., daily or weekly monitoring);

* Update the status of the air handling system diagram for ~~~ filtered air;
* Update the status of the new procedures for monitoring the repairs of ~~~ filters;
* Describe the increased frequency for gathering air samples specified in ST011;
* Include the SOP describing the frequency of checking the temperatures or for maintaining temperature records for the media storage area;
* Define the schedule for the routine calibration of the pressure gauges.

Sincerely,

James A. Rahto
Director
Minneapolis District

LRM/ccl